quinsy; also for those minor surgical operations associated with midwifery, when the more elaborate apparatus required for the administration of nitrous oxide and oxygen or cyclopropane is not available.

Cyclopropane (C₃H₆)

This comparatively new anaesthetic has a definite place in anaesthesia for minor surgery, as premedication can be dispensed with entirely, although it is an advantage to administer small doses such as 1/100 grain of atropine and 1/6 grain of morphine. It is not unpleasant from the patient's point of view, and any stage of anaesthesia required can be quickly and easily produced, although the profound relaxation of deep ether or spinal anaesthesia cannot be obtained. Complete and absolute recovery with cyclopropane is rapid; post-operative complications are rare, with the exception of vomiting, which, strange to relate, is usually unassociated with nausea and does not distress the patient to any extent.

Cyclopropane cannot be classified as an entirely safe anaesthetic, although, unlike chloroform, some warning of impending disaster is certainly given by failure of respiration, rapidly increasing pulse rate, or a pulse rate below 50; but, owing to its quick elimination, it is easy, by washing out or diluting the anaesthetic with oxygen, to get the patient to a lighter and safer plane of anaesthesia. The high cost of this gas makes it essential that it be administered always by a close-circuit system, of which there is no standard pattern in Britain at the moment; but many types of apparatus are being experimented with, and it is possible that in the near future an apparatus which is easily portable, efficient, and moderately inexpensive will be on the market.

Conclusion

From these remarks on the relative merits of the various anaesthetic agents at our disposal for administration in minor surgical procedures it is obvious that no one drug is much in advance of the others in efficiency and safety, and that choice of the anaesthetic must depend on the surgical operation to be performed and the social and economic conditions of the patient. In conclusion it might well be stressed that so-called minor surgical proceedings require as much skill and ability on the part of the anaesthetist as major operations where the patient has been properly prepared, examined, and premedicated. Too often does one hear a surgeon tell a patient that a mere whiff of anaesthetic is all that is necessary before, say, a manipulation which we all know requires full and profound surgical anaesthesia.

A. Jores (*Med. Welt*, October 2, 1937) discusses the relations between the hypophysis and renal affections as met with in pregnancy, in eclampsia, in Cushing's syndrome, and in nephritis. There seems to be a connexion between the basophil cells of the hypophysis and increased blood pressure. It has been proved experimentally on rabbits that the administration of large doses of extract of the posterior lobe of the pituitary gives rise to patches of necrosis in the liver and to changes in the kidneys similar to those observed in eclampsia. On the other hand, in about one-third of the cases of Cushing's syndrome the kidneys showed histological evidence of sclerosis at the post-mortem examination. Similarly there seems to be a definite connexion between acute nephritis and the system composed of the hypophysis and the middle brain. The author, however, warns against exaggeration of the importance of the hypophysis in renal affections.

VISCERAL PAIN*

BY

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The subject of visceral pain is a large one and some limitation of my subject is essential. We can consider visceral pain first as Nature's danger-signal, and our most valuable aid to diagnosis. This involves a determined attempt to unravel and understand its mechanism, for we may be sure that if we cherish any illusions as to that mechanism our diagnosis will go astray. But there is an alternative and no less necessary point of view. We may consider visceral pain not as a warning, grim at times, yet on the whole beneficent, but as a calamity from which our patients implore us to deliver them. When the pain originates in a hopeless condition such as an inoperable carcinoma of the rectum or intractable angina pectoris, though the surgeon must still be familiar with the nervous pathway by which the pain is transmitted to the sensorium, he is less concerned with what he can learn from that pain than with what he can do to relieve it. I propose, therefore, to limit my remarks to the mechanism of visceral pain from its diagnostic aspect, and to deal for the most part with pain originating in the gastro-intestinal tract.

The problem here is a peculiar one, differing, for instance, from that of pain in the genito-urinary system, since the gastro-intestinal tract is quite insensitive to the stimuli—cutting, burning, etc.—which cause pain when applied to the somatic nerves, and yet is supplied with afferent nerve fibres capable of causing direct visceral pain in response to an adequate stimulus. We have quite discarded, I think, the theory of Lennander that there is no such thing as true visceral pain in the gastro-intestinal tract, and also the theory of Mackenzie that all pain in gastro-intestinal lesions is referred to the somatic nerves of the abdominal wall. The one stimulus adequate to produce direct visceral pain in the gastro-intestinal tract appears to be tension on the afferent nerves in its muscular coats, and this tension is usually caused by spasmodic and exaggerated peristaltic contraction.

The afferent nerves supplying the insensitive intra-peritoneal viscera show no anatomical features that distinguish them from the somatic sensory nerves, but their physiological limitations are so striking that we are justified in regarding them as a separate system, to which we may perhaps give the name of viscerosensory nerves. It must not be forgotten that the mesentery and mesocolon are supplied by somatic sensory nerves to within a short distance of their attachment to the bowel, though the great omentum appears to be devoid of any sensory nerves subserving pain. The sensitive mesentery is often involved in such lesions as strangulation and volvulus, and this causes a combination of visceral and somatic pain that is not easy to unravel.

Characteristics of Pure Visceral Pain

We can study the features of visceral pain in the intestine in its purest form in strangulation of a small knuckle of the lower small intestine in a femoral hernia. I insist that the knuckle must be a small one, because then the sensitive portion of the mesentery is not involved. Another equally good lesion for our purpose is a stenosing

* Read in opening a discussion in the Section of Anatomy, Physiology, and Biochemistry at the Annual Meeting of the British Medical Association, Belfast, 1937.

cancer of the transverse or pelvic colon, causing a high grade of obstruction. In both conditions the pain occurs in intermittent spasms lasting half a minute or so, and repeated at regularly recurring intervals. Where the obstruction is of some days' standing, with each spasm of pain hypertrophied coils of bowel above the obstruction may be both felt and seen in abnormally vigorous peristalsis, demonstrating in a most convincing manner the mechanism by which the pain is caused.

If, then, we interrogate and examine a patient suffering from such a visceral pain we find that it is felt as a central pain and not on the surface of the abdomen. We also find that it is quite vaguely localized, though in the case of the small-intestine strangulation it is localized at or above the level of the umbilicus, whereas in cancer of the colon, whether in the transverse or pelvic portion, the patient points to the hypogastrium as the seat of the pain. Physical examination reveals a complete and remarkable absence of objective somatic manifestations. We find no superficial hyperalgesia, no deep tenderness, and no muscular rigidity, and movement of the abdominal wall does not accentuate the pain, so that the patient often writhes about in a vain attempt to obtain relief.

That is the picture of the purest and most certain visceral pain in the gastro-intestinal tract that we know. A similar picture is seen in the early hours of an attack of acute appendicitis with obstruction of the lumen of the appendix. Here, too, we find the same vaguely localized central pain and the same absence of any somatic manifestations such as tenderness and rigidity.

On the other hand, where an abdominal pain is associated with reflex muscular rigidity and with deep tenderness on palpation, the strict localization of this rigidity and tenderness suggests a somatic origin for the reflexes. We see this most convincingly in acute appendicitis, where the site of the second pain in the right iliac fossa, with its corresponding area of tenderness and rigidity, varies from case to case with the position in which the appendix happens to be lying; so that in almost every case before we operate we can predict where the inflamed appendix will be found.

I have argued before that these clinical facts drive us to the inevitable conclusion that the nerves of the sensitive parietal peritoneum must receive the stimulus that gives rise to the pain and tenderness in the superficial parts of the abdominal wall and to the associated reflex muscular rigidity, and I have described the process as peritoneo-cutaneous radiation and a peritoneo-muscular reflex. An appreciation of this peritoneo-cutaneous radiation is essential for any true understanding of abdominal pain, and the mechanism is best illustrated by stimulation of the phrenic nerve terminals below the diaphragm. When the under-surface of the central portion of the diaphragm receives a painful stimulus immediate pain is felt in the region of the descending branches of the third and fourth cervical nerves supplying the skin of the supra-acromial region. The following experiment, typical of many, demonstrates both the extreme sensitivity of the afferent nerve fibres and the essential features of referred pain.

A man 20 years of age was operated on for chronic appendicitis under spinal anaesthesia, which extended to the fifth dorsal segment. Pressure with a gloved finger was made on the under-surface of the right dome of the diaphragm in its anterior central part. The patient immediately complained of sharp pain over the front of the centre of the right clavicle. The skin in this area was lightly pinched, and was hyperalgesic. Immediately the stimulation of the diaphragm was stopped the pain and

hyperalgesia disappeared. No pain was felt in the region of the diaphragm. A hand was then introduced behind the bare area of the liver and the diaphragm pressed upon with a finger in its posterior part. Pain was at once complained of over the suprascapular region, and the skin in this area was also found to be hyperalgesic. Again on ceasing to stimulate the diaphragm the pain disappeared, and with it the hyperalgesia, though two or three minutes later the patient complained of a transient return of the pain and soreness, lasting a minute or so.

I have shown that infiltration with novocain of the area of skin supplied by the third, fourth, and fifth cervical nerves either abolishes or greatly modifies the referred pain caused by stimulation of the diaphragm (Morley, 1931). The experiment has been indirectly criticized (Woollard, Roberts, and Carmichael, 1932), but it has been several times repeated, and the fact must be accepted as established. The mechanism of this shoulder-tip pain is a matter of extreme interest. It is beyond question purely somatic, since the third, fourth, and fifth cervical segments of the cord have no neural connexions with the abdominal viscera. The theory that has commonly been held to explain it is that propounded by James Ross of Manchester (1888)—the theory of an irritable focus in the spinal cord. I have long pointed out the objections to Ross's theory of the diffusion of pain through an irritable focus in the cord so far as the viscerosensory nerves from the gastro-intestinal tract are concerned, but have reluctantly held to it as a working hypothesis to explain this shoulder-tip pain from phrenic stimulation. My reluctance has been based on the complete absence of any real physiological evidence in support of such a mechanism—any crucial test of its existence.

An Alternative to the "Irritable Focus" Theory

Recent experimental work on action currents combined with division of the posterior nerve roots would seem to provide us with a simpler and more rational explanation of this peritoneo-cutaneous radiation of pain. Barron and Matthews (1934-5) have shown that some 40 per cent. of the posterior root fibres of the spinal nerves can carry centrifugal impulses. Of these a large proportion start in a peripheral sense organ and run to the cord. There one collateral (or more) passes a long or a short distance up or down the cord and leaves it again by a different rootlet from that containing the entrant fibre, though it may be in the same or a different posterior root. It then passes to the periphery, often to a point far distant from the original sense organ. Barron and Matthews found that of fibres entering the cord by the posterior roots more than half send collaterals out to the periphery via a posterior rootlet different from that by which they enter.

They have found, further, that when a single afferent fibre in a posterior spinal rootlet is stimulated the impulse emerges through its efferent collateral or collaterals in other rootlets with no more delay than can be ascribed to conduction time. This observation gives confirmatory evidence that the efferent fibres referred to are collaterals of the posterior root ganglion cells, and that no synapse is interposed in their course within the central nervous system. Yet despite this absence of a synapse, inhibition or modification of impulses within the central nervous system was proved, since discharges enter the cord as a continuous series of impulses and leave it as an intermittent series.

It is plain that the old conception of the posterior root fibres as purely afferent in function is no longer tenable.

This recent discovery of efferent collateral fibres in continuity with the cells of the posterior root ganglia appears to me to give us a probable key to the mystery of peritoneo-cutaneous radiation of pain, without any violation of the law of forward conduction associated with the names of Bell and Magendie. Is it not probable that, on stimulation of the phrenic nerve, efferent fibres in the posterior roots run down to the skin supplied by the third, fourth, and fifth cervical segments, and there liberate a chemical metabolite which stimulates the endings of adjacent pain fibres in the skin (see diagram)? The work of Sir Thomas

Diagram showing possible mechanism of referred pain on stimulation of phrenic afferent fibre in diaphragm (D). The sensory nerve from the skin of the shoulder is not depicted.

Lewis has made us familiar with the conception of pain as due to the action of a chemical substance on the sensory nerve endings. But it is plain that the nocifensor system of nerves postulated by Lewis (1937) cannot be held responsible, since the hyperalgesia produced in his experiments took many minutes to develop and persisted many hours, whereas shoulder-tip pain and its associated hyperalgesia develop instantly when the phrenic nerve is stimulated, and when the stimulus is removed they almost as instantaneously disappear. In the pain that we are considering the reaction that occurs in the skin is both rapid and reversible.

Such a mechanism as I have suggested would provide a simple explanation of the referred pain felt on stimulation of the phrenic nerve and its modification by anaesthetizing the skin without any need for invoking the theory of an irritable focus in the spinal cord. One would hazard the guess that the afferent nerves from the gastrointestinal tract may prove to be devoid of efferent collateral fibres running out to the superficial layers of the abdominal wall, and that this discovery, when it is made, will add an anatomical feature to the physiological argument for regarding them as a special group of nerves.

Peritoneo-cutaneous Radiation in the Abdominal Wall

A study of phrenic pain leads us inevitably to the conclusion that a precisely similar peritoneo-cutaneous radiation occurs in the superficial nerves of the anterior

abdominal wall when the underlying parietal peritoneum receives a painful stimulus from an inflamed viscus or inflammatory exudate. Infiltration experiments with novocain again confirm this conclusion. It is easily demonstrated, for instance, that the localizing pain in acute appendicitis or acute cholecystitis is greatly modified or completely abolished by inducing local anaesthesia by subcutaneous infiltration of the area in which the pain is felt. These experiments have been urged in support of Mackenzie's theory of a viscerosensory reflex (Weiss and Davis, 1928); yet, as we have seen, there are good reasons for the belief that the visceral afferent nerves are in no way involved, but only the afferent nerves from the parietal peritoneum.

The sensitivity of the parietal peritoneum is so extreme that it is hardly adequate to say that it reacts to the stimuli that produce pain on the surface of the body. The fact that we can elicit pain by touching the diaphragm with a gloved finger, and the occurrence of severe peritoneal pain from effusions of blood and blood clot in the intraperitoneal haemorrhage, demonstrate that the sensitivity of the parietal peritoneum is more closely analogous to that of the cornea than to that of the skin.

Definition of Referred Pain

Holding as I do that true visceral pain in the intraperitoneal organs is in no sense projected to the surface of the body, and that Mackenzie's theory of a viscerosensory and visceromuscular reflex is unsound so far as these organs are concerned, I suggest that a more precise and just definition of referred pain is required. That much-abused term is commonly held to mean pain felt at a point remote from the seat of stimulation. Under this definition the hypogastric pain resulting from a carcinoma of the splenic flexure of the colon would be a referred pain, but I have already argued that it is merely imperfectly localized and in no sense referred. I suggest, therefore, that we limit the term "referred pain" to pain resulting from stimulation of a somatic sensory nerve and referred to a remote part of the distribution of that nerve or of the segmental sensory distribution with which it is connected. This definition covers such well-known examples of referred pain as that felt in the knee in disease of the hip-joint, or as the striking experiment of Sir Thomas Lewis in which stimulation of nerve endings inside his maxillary antrum caused referred pain and hyperalgesia in the whole distribution of the second division of the trigeminal nerve.

Referred Pain in the Urinary System

Under this more precise definition of referred pain we must include pain radiating to the testis resulting from renal or ureteric colic, or felt in the end of the urethra from stimulation of the trigone of the bladder. It must here be emphasized that the interior of the pelvis of the kidney and the ureter are sensitive to mechanical stimuli, as is the base of the bladder. These organs are therefore, by definition, innervated with sensory nerves of a different physiological group from the afferent nerves of the gastrointestinal tract, since they respond to the common type of pain stimulus. Thus it need cause us no surprise that they should give rise on stimulation, as they undoubtedly do, to both visceromuscular reflexes and viscerocutaneous referred pain.

Angina Pectoris

A very limited personal experience of this condition precludes me from speaking with authority on the mechanism of pain in angina pectoris, but I must refer

briefly to an important recent contribution by J. C. White of Boston (1935) on this subject. White has shown that the pain of angina pectoris and of aneurysm of the aortic arch can be abolished by injection with alcohol or surgical excision of the upper five thoracic sympathetic ganglia and by division of the upper five posterior thoracic spinal roots. Experimental confirmation was obtained in dogs. By passing a silk ligature under the left coronary artery and bringing it out through the chest wall in a glass tube, temporary occlusion of the coronary could be produced with ease, and gave rise to obvious signs of cardiac distress within a few seconds. When the four upper pairs of thoracic ganglia were excised, or the upper five pairs of posterior spinal roots divided, the occlusion caused no manifestations of distress. Division of the vagi, the upper six intercostal nerves, and bilateral stellate ganglionectomy all failed to prevent the discomfort, and it is plain that the afferent pain fibres from the heart pass through the thoracic cardiac nerves entering the upper five thoracic segments.

White believes that cardio-aortic pain is produced in part by the viscerocutaneous reflex postulated by Mackenzie, but also in large part by direct transmission over visceral afferent pathways, or, in other words, as a true visceral pain. He gives both clinical and experimental evidence against the axon reflex as a factor in cardiac pain.

Dual Mechanism of Abdominal Pain

Whatever the ultimate truth may be as to the mechanism of referred pain in angina, I think we must admit the probability that it differs fundamentally from the mechanism of pain in the gastro-intestinal tract. In that tract we have certainly a dual mechanism. On the one hand we see true visceral pain as part of a defence against the threat of obstruction. It is primitive in the scale of evolution, is in no sense referred to the superficial somatic nerves, and is imperfectly and vaguely localized. On the other hand we find referred pain, the stimulus for which arises not from the visceral afferent nerves at all but from the somatic nerves of the parietal peritoneum. It has been evolved as a protection against bacterial infection of the peritoneum, either by penetrating wounds from without or by perforation of the intestine within. It is later in the scale of evolution, and produces a radiation of pain to the superficial somatic nerves and a reflex protective rigidity of the overlying muscles, both of which are accurately localized.

REFERENCES

- Barron, D. H., and Matthews, B. H. C. (1934-5). *J. Physiol.*, **83**, 5P.
 — (1935). *Ibid.*, **84**, 9P.
 Lewis, Sir T. (1937). *British Medical Journal*, **1**, 431.
 Morley, J. (1931). *Abdominal Pain*, Edinburgh.
 Ross, J. (1888). *Brain*, **10**, 352.
 Weiss, S., and Davis, D. (1928). *Amer. J. med. Sci.*, **176**, 517.
 White, J. C. (1935). *Ass. Res. nerv. and ment. Dis.*, **15**, 181.
 Woollard, H. H., Roberts, J. E. H., and Carmichael, E. A. (1932). *Lancet*, **1**, 337.

In a report issued as Water Pollution Research Technical Paper No. 6 by the Department of Scientific and Industrial Research (H.M. Stationery Office, 12s. 6d.) a detailed description is given of the results of a chemical and biological investigation of the non-tidal reaches of the River Tees. This investigation, which occupied about four years, formed part of a comprehensive chemical, biological, and hydrographical survey of the whole of the river and its tributaries from its source to the sea. The object of the survey was to obtain data on the effects of the various discharges of sewage and trade effluents on the river and on the extent to which these liquids should be purified before discharge if serious pollution of the river water is to be avoided.

BRUCELLOSIS IN MAN AND ANIMALS IN STAFFORDSHIRE LABORATORY OBSERVATIONS

BY

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The incidence, bacteriology, and epidemiology of undulant fever vary in different countries. In many lands the disease is more prevalent than in Great Britain. On the Mediterranean littoral *Br. melitensis* predominates. In the United States of America *Br. melitensis*, *Br. suis*, and *Br. abortus* all occur. In this country *Br. abortus* prevails. The animal vectors also show geographical variation. In southern Europe the goat is pre-eminent. In America the goat, pig, cow, and sheep play a part. In England the cow is considered the main reservoir of infection, for although horses suffering from poll evil and fistulous withers also harbour *Brucella* they are not regarded as of grave epidemiological importance. While these fundamental differences are clearly recognized and accepted, there are other discrepancies which arise from unstandardized and varied techniques. Also a great deal of work remains to be done in this country on the comparative aspects of brucellosis in relation to human infection, and the findings and conclusions of distant authorities are often accepted too readily as applying universally.

The aims of this local investigation were: (A) to ascertain the prevalence of agglutinins to *Brucella* in the sera of man and of some of the animals presumed to have been in contact with infected cattle; (B) to assess the accuracy of the agglutination test as a diagnostic procedure; (C) to find out the incidence of *Brucella* organisms in the milk of the cow and of the goat; (D) to investigate the species and virulence of the organisms recovered.

A. Serological Investigations

Three different antigens were used in this investigation: standardized Oxford suspensions; a local laboratory strain; and the special antigen used by Huddleson (1932) in his rapid method of field testing.

Human Sera.—These specimens consisted of two groups: (I) those taken from patients suffering from or with a recent history of an infection causing pyrexia and submitted to the laboratory for the routine Widal reaction; (II) those from people with no history of recent infection with fever.

Group I comprised 500 sera. Fifty reacted to *Br. abortus*, ninety-eight to different members of the typhoid-paratyphoid-salmonella-dysentery group, and the remainder were completely negative to all the twenty-seven micro-organisms used in the routine tests. The fifty sera agglutinating *Br. abortus* reacted in the following titres:

TABLE I

1/25	1/50	1/125	1/250	1/500	1/1,250	1/2,500	1/5,000
6	9	5	2	5	15	4	4

Group II consisted of two batches of 500 sera, one examined in 1932-3 and the other in 1937. They reacted to *Br. abortus* in the following numbers and dilutions:

TABLE II

Years	1/25	1/50	1/125	1/500	Negative
1932-3	—	1	3	1	495
1937	3	2	—	—	495